A Comparative Study of YOLO-based Architectures for Mitosis Detection in Histopathology Images

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Abstract. Mitosis detection is a crucial task in tumor grading and prognosis assessment, especially in breast cancer diagnosis. However, manual identification of mitotic cells in Hematoxylin and Eosin (H&E) stained histopathological images is time-consuming, subjective, and labor-intensive. Automated computer-aided diagnosis systems can significantly support pathologists by improving efficiency and consistency. In this study, we present a comprehensive comparative evaluation of several YOLO-based one-stage deep learning architectures for mitosis detection. Specifically, YOLOv8, YOLOX, YOLOv11, and YOLOv26 are assessed on three publicly available datasets: ICPR12, ICPR14, and MiDeSeC. The models are evaluated using precision, recall, and F1-score to ensure a balanced performance comparison. Experimental results indicate that YOLOv8 consistently achieves strong performance across all datasets, demonstrating robustness and reliability. Overall, the results suggest that modern YOLO-based detectors provide competitive performance for automated mitosis detection and represent a promising direction for further research and practical development.

Keywords: Mitosis detection · Histopathological image · Object detection · YOLO.

1 Introduction

Mitosis is the biological process in which a cell divides into two genetically identical daughter cells and represents a fundamental mechanism of cellular proliferation. During this process, the genetic material is duplicated and equally distributed between the two newly formed cells. In histopathology, the presence and number of mitotic figures provide important information about the proliferation activity of tumor cells [1]. The mitotic count is therefore widely used as a key criterion in tumor grading systems, particularly in breast cancer diagnosis. Tumors with a high number of mitotic figures generally indicate increased proliferative activity and are often associated with more aggressive tumor behavior

and poorer prognosis. For this reason, accurate identification and quantification of mitotic cells in histopathological images play a critical role in determining tumor grade and guiding clinical decision-making [2].

Despite its clinical importance, the detection of mitotic figures in Hematoxylin and Eosin (H&E) stained histopathological images is a challenging task. Mitotic cells appear relatively rarely compared to other cellular structures and often show significant morphological variability during different phases of cell division. In addition, mitotic figures can be visually similar to non-mitotic structures such as apoptotic cells, inflammatory cells, and staining artifacts. These factors make manual identification difficult, time-consuming, and prone to inter-observer variability among pathologists. Consequently, automated approaches for mitosis detection have attracted significant research attention [3]. Early studies on mitosis detection mainly relied on traditional image processing and machine learning techniques. These methods generally involve preprocessing steps such as color normalization, segmentation, and handcrafted feature extraction based on morphological, texture, or intensity characteristics. The extracted features are then classified using machine learning algorithms such as Support Vector Machines (SVM), Random Forests, or k-Nearest Neighbors (k-NN). Although these approaches have demonstrated promising results in certain cases, their effectiveness largely depends on the quality of manually designed features. Moreover, handcrafted feature-based methods often struggle to capture the complex appearance and variability of mitotic figures in histopathological images, which limits their generalization capability across different datasets and staining variations [4].

Numerous studies have investigated mitosis detection using deep learning techniques. Among these, recent YOLO-based approaches have become particularly prominent due to their ability to perform accurate and efficient object detection in complex histopathological images [4]. Xiao et al. [6] proposed a two-stage mitosis detection framework that combines an improved YOLO11x detector with a ConvNeXt classifier. In this framework, the first stage generates mitosis candidates, while the second stage filters false positives to improve detection precision; however, the two-stage pipeline increases computational complexity. Ardac and Erdogmus [7] introduced Mi-DETR, a DETR-based mitosis detection model that replaces the original backbone with CSPResNeXt-50, reduces decoder layers for efficiency, and employs CIoU loss to improve bounding-box regression. Despite these improvements, transformer-based architectures may still miss mitotic cells in challenging regions. Makhdoom et al. [8] proposed a YOLOv8-based pipeline that divides whole-slide images into patches, applies stain normalization, and performs detection using a one-stage YOLO model, achieving high detection accuracy and fast inference. Sheikh et al. [9] introduced IHA-YOLO, which incorporates an inter-head self-attention mechanism to enhance feature representation and improve detection of small cells. Lei et al. [10] proposed a cascade detection framework that first segments cell nuclei using an improved VNet model and then classifies candidate regions using a CNN; however, its performance may still be affected by complex tissue backgrounds and visually similar non-mitotic cells. Bourgade et al. [11] proposed a YOLOv12-based framework

for pan-cancer mitosis detection that improves robustness through stain normalization, data augmentation, and tile-based processing, although detection performance may still be sensitive to domain shifts. Finally, Topuz et al. [12] proposed SDF-YOLO, a YOLOv11-based framework that employs a single detection head and coordinate attention to better capture small targets, achieving improved detection accuracy across multiple datasets, although its generalization capability still requires further validation.

Despite these advances, most existing studies focus on improving a specific detection framework rather than systematically comparing different YOLO-based architectures. As a result, there is limited understanding of how recent YOLO models perform relative to each other for mitosis detection under consistent experimental conditions. A comprehensive comparative analysis can therefore provide useful guidance for researchers in selecting appropriate detection models for histopathological image analysis.

In this study, a comparative analysis of mitosis detection using YOLO-based one-stage deep learning models on H&E breast cancer histopathological images is presented. The primary objective is to evaluate the performance of different YOLO architectures on mitosis datasets and to compare their effectiveness in terms of F1-score. In addition, a preprocessing strategy, including patch extraction and data augmentation strategies, is applied to enhance the representation of small mitotic structures and improve detection performance. The experimental results indicate that YOLO-based approaches can provide competitive detection performance, demonstrating their potential for integration into computer-aided diagnosis systems for automated mitosis detection.

2 Datasets and Proposed Method

2.1 Datasets Used in the Study

In this study, we selected three publicly available datasets for mitosis detection:

a) The ICPR12 dataset [13] consists of 50 high-power fields (HPFs) extracted from five H&E-stained breast cancer whole-slide images, with all mitotic figures manually annotated. Each HPF covers an area of 512 $\mu m \times 512$ μm (0.262 mm^2), corresponding to image sizes of approximately 2084×2084 pixels, depending on the scanner resolution. The slides were digitized using two RGB whole-slide scanners and a multispectral microscope providing 10 spectral bands and 17 Z-stack layers, resulting in a total of 326 annotated mitotic cells. This dataset provides a diverse and challenging benchmark for evaluating robust and generalizable mitosis detection algorithms.

b) The ICPR14 dataset [14] is a standard benchmark for mitosis detection in breast cancer histopathology images, containing 1,696 high-resolution patches, of which 1,200 are labeled. Annotations indicate only the approximate centers of mitotic figures, without precise segmentation masks. Although this weak labeling increases detection difficulty, the dataset remains widely used due to its historical importance and its role in the development of deep learning mitosis detection methods.

c) The MiDeSeC dataset [15] was constructed using H&E breast cancer tissue slides obtained from 25 anonymized cases. Whole-slide images were acquired using a 3D HISTECH Panoramic Scanner P250. Expert pathologists annotated invasive tumor regions, excluding benign tissue, stromal areas, and artifacts. From the selected tumor regions, 1024×1024 pixel image patches were extracted in RGB 8-bit format. Typical and atypical mitotic figures were manually labeled using the QuPath software. The final dataset includes annotated image patches and corresponding coordinate files, and it was randomly divided into training (two-thirds) and testing (one-third) subsets for deep learning experiments.

2.2 Proposed Method

The overall workflow of the proposed mitosis detection method is illustrated in Fig. 1. First, the original polygon annotations are then converted into bounding box format so that they can be used with YOLO-based object detection models. After annotation preprocessing, large microscopy images are divided into smaller patches using a sliding-window approach. The generated patches are filtered so that only those containing mitosis samples are retained. To increase the diversity of the training data, several data augmentation techniques are applied, including rotation, flipping, scaling, cropping, and mosaic augmentation. The patches are then resized before being used for model training. Finally, several YOLO-based architectures are trained and evaluated using standard detection metrics such as precision, recall, and F1-score.

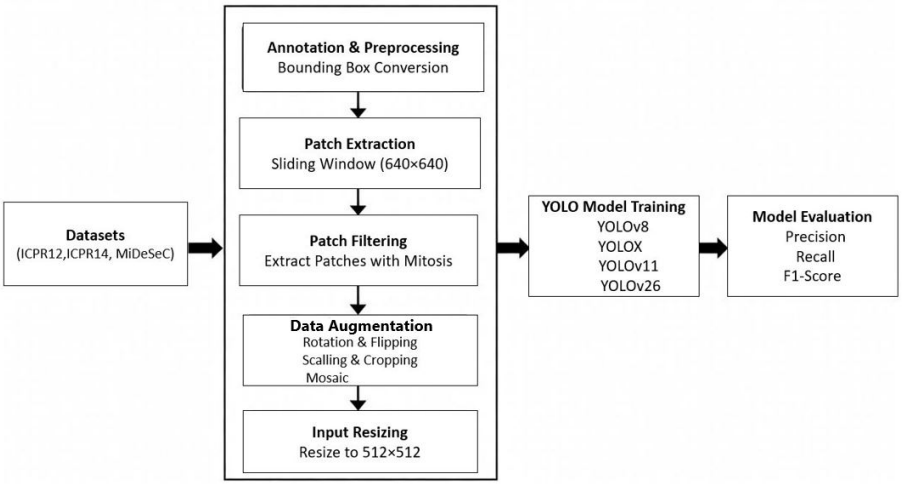

Fig. 1. The workflow for mitosis detection.

Preprocessing In this study, preprocessing was performed in several steps before model training. First, the original polygon-based manual annotations were converted into bounding box format to make them compatible with YOLO-based object detection models. For each mitotic cell, the minimum and maximum polygon coordinates were used to generate the smallest enclosing bounding box, and all coordinates were normalized to the $[0, 1]$ range according to the image dimensions. Second, the predefined test sets provided by the datasets were kept unchanged and used directly for evaluation, while the remaining images were used for training and validation, with 80% used for training and 20% reserved for validation. Third, to process the large microscopy images and improve the detection of small mitotic figures, a sliding-window slicing strategy with overlap was applied. Each image was divided into 640×640 pixel patches, using an overlap ratio of 60% for the training set and 10% for the validation set. This helped reduce the risk of missing mitotic cells near patch boundaries and increased data diversity. Fourth, during patch extraction, only objects whose bounding boxes overlapped with a patch by at least 30% were retained, and their coordinates were transformed into the local patch coordinate system and normalized again. Fifth, the generated patches were resized to 512×512 pixels before training to reduce computational cost while preserving the main morphological characteristics of mitotic cells. Sixth, to reduce the dominance of background regions, patches containing mitotic cells were prioritized during dataset construction. Finally, several augmentation techniques were applied during training, including random rotation, horizontal and vertical flipping, mosaic augmentation, random scaling, and random cropping. These preprocessing steps increased data diversity and supported more robust mitosis detection.

Mitosis Detection In the detection stage, YOLO-based object detection models were used to identify mitotic cells in histopathological images. The extracted image patches served as inputs to the models, which were trained to predict bounding boxes corresponding to mitotic figures. Due to their single-stage detection framework and effective multi-scale feature learning, YOLO architectures are well suited for detecting small objects within complex tissue structures. To evaluate the suitability of YOLO-based approaches for mitosis detection, four different architectures were investigated:

YOLOv8 [16]: YOLOv8 is an anchor-free object detection model that improves the localization of small objects through optimized feature extraction and multi-scale feature fusion. Its PAN-FPN neck structure combines information from different feature levels, which helps detect small mitotic cells across varying image resolutions.

YOLOX [17]: YOLOX introduces a fully anchor-free detection framework with a decoupled head that separates classification and localization tasks. This design improves detection accuracy, especially for small and densely distributed objects such as mitotic figures in histopathology images.

YOLOv11 [18]: YOLOv11 follows the typical YOLO architecture consisting of a backbone, neck, and detection head. The backbone extracts hierarchical

feature representations from the input images, while the neck integrates multi-scale features using FPN and PAN structures. The decoupled detection head separately handles classification and bounding box regression, improving training stability and localization performance.

YOLOv26 [19]: YOLOv26 is designed as an efficient object detection framework suitable for real-time applications. It uses a lightweight backbone for feature extraction and a compact neck for multi-scale feature fusion. The detection head performs direct regression without relying on traditional non-maximum suppression, enabling faster inference while maintaining competitive detection accuracy.

3 Experiment Settings

All experiments were conducted on a workstation equipped with an NVIDIA RTX 4000 GPU, an Intel(R) Xeon(R) W-2245 CPU @ 3.90 GHz, and 64 GB of system RAM. The models were implemented in Python. For all YOLO-based architectures, the training configuration used an initial learning rate of 0.001, 100 training epochs, and a batch size of 8 with the AdamW optimizer. Early stopping was applied with a patience value of 25, meaning that training was automatically terminated if no improvement in validation performance was observed for 25 consecutive epochs.

The performance of the models was evaluated using Precision, Recall, and F1-score. Precision measures the proportion of correctly detected mitotic cells among all detections, while Recall reflects the ability of the model to identify true mitotic cells. The F1-score combines Precision and Recall, providing a balanced measure for evaluating mitosis detection performance.

4 Experiment Results

4.1 Results of YOLO-based Models

The F1-score results of the YOLO-based architectures on the MiDeSeC, ICPR12, and ICPR14 datasets are presented in Table 1. Overall, YOLOv8 achieved the best performance across all datasets. With preprocessing, YOLOv8 obtained the highest F1-scores on MiDeSeC (0.712), ICPR12 (0.766), and ICPR14 (0.70). These results indicate that YOLOv8 provides a stronger balance between precision and recall and is more effective in detecting small mitotic figures in histopathological images. YOLOX, YOLOv11, and YOLOv26 produced consistently lower F1-scores across all datasets compared to YOLOv8. Although these models achieved reasonable detection performance, their results remained below those of YOLOv8 in both preprocessing settings. Among them, YOLOX generally performed slightly better than YOLOv11 and YOLOv26, particularly on the ICPR12 dataset. YOLOv11 showed stable results across datasets, while YOLOv26 achieved competitive but relatively lower performance.

Table 1. F1-score results of YOLO-based architectures with(out) preprocessing.

Model	Without Preprocessing			With Preprocessing		
	MiDeSeC	ICPR12	ICPR14	MiDeSeC	ICPR12	ICPR14
YOLOv8	0.64	0.73	0.678	0.712	0.766	0.70
YOLOX	0.61	0.678	0.65	0.66	0.695	0.67
YOLOv11	0.62	0.659	0.65	0.664	0.689	0.67
YOLOv26	0.63	0.65	0.63	0.674	0.684	0.657

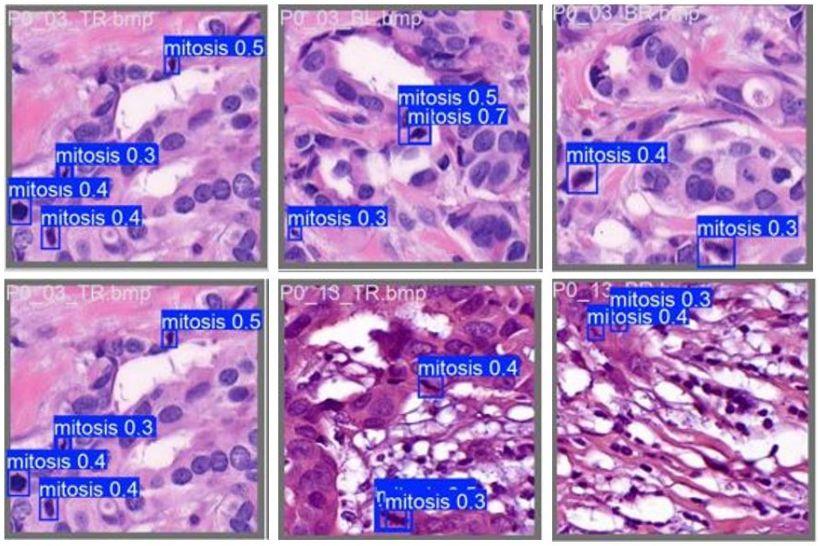

Fig. 2. Illustrative results of YOLOv8.

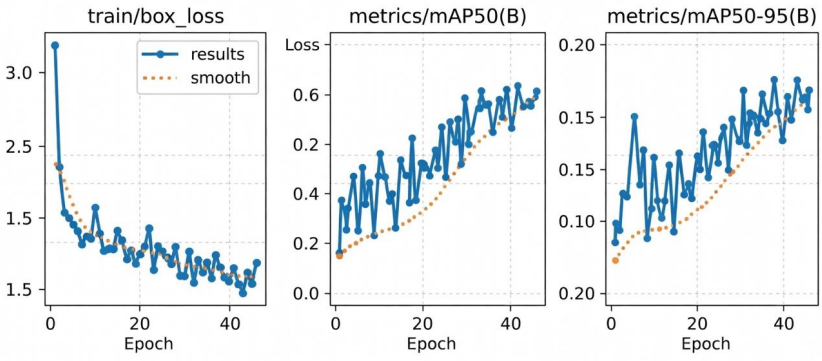

Fig. 3. Training and validation performance analysis of YOLOv8.

The impact of the proposed preprocessing strategy is also clearly observed in Table 1. For all models and datasets, preprocessing consistently improved the F1-score. For example, the F1-score of YOLOv8 increased from 0.64 to 0.712 on MiDeSeC and from 0.73 to 0.766 on ICPR12 after applying preprocessing. Similar improvements are observed for YOLOX, YOLOv11, and YOLOv26. These results suggest that the proposed preprocessing approach, which includes overlapping sliding-window patch extraction and data augmentation, improves the representation of small mitotic structures and reduces the risk of missing objects near patch boundaries.

In general, the ICPR12 dataset yielded the highest F1-scores across all models, while MiDeSeC produced slightly lower scores. This difference may be related to variations in staining conditions, image resolution, and cellular morphology across the datasets, which influence the difficulty of mitosis detection. Overall, the results demonstrate that the proposed preprocessing strategy consistently improves detection performance, while YOLOv8 provides the most effective architecture for mitosis detection among the evaluated models. Furthermore, some illustrative results of the YOLOv8 model are provided in Fig 2.

The training curves are shown in Fig. 3, including the box regression loss, mAP50, and mAP50–95 across training epochs. The training curves indicate a stable learning process throughout the epochs. The box regression loss decreases steadily during training, showing that the model progressively improves its ability to localize mitotic cells. At the same time, both mAP50 and mAP50–95 metrics increase consistently, indicating improved detection performance and more accurate bounding box predictions. Although minor fluctuations are observed, the overall trends demonstrate effective convergence of the model and stable training behavior without signs of instability.

4.2 Comparisons with Recent Works

This section evaluates the performance of the proposed YOLO-based approach in comparison with recent studies on mitosis detection. Tables 2 and 3 present a comparative analysis of the proposed method and recently introduced approaches across multiple datasets.

The results in Table 2 show that the proposed method achieves competitive performance compared with existing approaches in the literature. The YOLOv8-based model obtains a high F1-score and clearly outperforms several earlier methods based on CNN features or handcrafted representations. Although some approaches, such as lightweight R-CNN, report slightly higher F1-scores, the proposed method still demonstrates strong detection capability using a modern object detection architecture. In addition, the comparison highlights the importance of data augmentation and model optimization strategies for improving mitosis detection performance.

Table 3 provides a broader comparison of different methods evaluated on the ICPR14 dataset. Earlier studies mainly relied on combinations of handcrafted features and CNN-based representations, while more recent works increasingly adopt deep learning–based object detection frameworks. Models such

Table 2. Comparison of different methods on ICPR12.

Study	Model	F1-score
Yancey. 2022[20]	YOLOR+ Data Augmentation	0.67
Dhivya & Vasuki. 2022 [21]	HC	0.6864
Das and Dutta. 2019 [22]	CNN	0.6523
Yucel et al. 2025 [23]	YOLOv5	0.73
Li et al. 2018 [24]	Lightweight RCNN	0.784
Proposed approach	YOLOv8	**0.766**

Table 3. Comparison of different methods on ICPR14.

Study	Model	F1-score
Vega et al.2023 [25]	YOLOX	0.68
Sohail et al. 2021[26]	MitosRes-CNN	0.75
Ali et al. 2021 [27]	(GLB-FPN) + focal loss (FL)	0.692
Mahmood et al. 2020 [28]	Faster R-CNN	0.691
Dodballapur et al. 2019 [29]	handcrafted + CNN features	0.64
Proposed approach	YOLOv8	**0.70**

as Faster R-CNN, MitosRes-CNN, and YOLOX illustrate the transition toward advanced detection architectures designed to better capture small and challenging objects. The comparison shows that the proposed YOLOv8-based method performs competitively with many recent approaches and improves upon several earlier methods that rely on handcrafted features. Although some specialized architectures report slightly higher performance, the results demonstrate that modern YOLO-based detectors remain effective solutions for mitosis detection in histopathological images.

5 Conclusion

This study presented a comparative evaluation of several YOLO-based object detection models for automated mitosis detection in histopathological images. Four architectures—YOLOv8, YOLOX, YOLOv11, and YOLOv26—were evaluated on three publicly available datasets: ICPR12, ICPR14, and MiDeSeC. The experimental results demonstrate that YOLO-based models can provide effective detection performance for mitotic figure identification in H&E-stained breast cancer images.

Among the evaluated models, YOLOv8 consistently achieved the most balanced performance across all datasets in terms of F1-score. This result suggests that architectures with strong multi-scale feature extraction and efficient feature aggregation are particularly suitable for detecting small objects such as mitotic cells. In contrast, although YOLOv26 represents one of the most recent YOLO architectures, its detection performance was lower than that of YOLOv8 in our experiments. This finding indicates that newer architectures do not necessarily guarantee better performance for specialized tasks such as mitosis detection.

Detecting mitotic figures remains a challenging problem due to their small size, visual similarity to surrounding cells, and the complex structure of histopathological tissue.

In addition, the proposed preprocessing strategy, including overlapping sliding-window patch extraction, patch-based dataset expansion, and extensive data augmentation, improved the detection performance of all evaluated models. These results highlight the importance of data-centric optimization strategies in improving the robustness and generalization ability of deep learning models for histopathological image analysis.

Future work will focus on extending the proposed framework to whole-slide image analysis, investigating domain adaptation techniques to improve cross-dataset generalization, and exploring hybrid architectures that combine object detection and segmentation-based methods for more precise localization of mitotic cells.

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Disclosure of Interests. The authors declare that they have no competing interests.

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